Efficient generation of hPSC-derived midbrain dopaminergic neurons in a fully defined, scalable, 3D biomaterial platform.

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Public Summary:
Human pluripotent stem cells, with their potential for indefinite self-renewal, may be an unlimited source of cells for a range of biomedical applications including regenerative medicine, drug screening and disease modeling. Parkinson's disease treatment is one key example where regenerative medicine could benefit from a large supply of the relevant transplantable cell-type, midbrain dopaminergic neurons. However, current methods of cell production is hard to scale up, and suffers from low reproducibility. To address these challenges, we present a method to efficiently generate large numbers of transplantable midbrain dopaminergic neurons in a fully-defined, scalable, 3D biomaterial platform.

Scientific Abstract:
Pluripotent stem cells (PSCs) have major potential as an unlimited source of functional cells for many biomedical applications; however, the development of cell manufacturing systems to enable this promise faces many challenges. For example, there have been major recent advances in the generation of midbrain dopaminergic (mDA) neurons from stem cells for Parkinson's Disease (PD) therapy; however, production of these cells typically involves undefined components and difficult to scale 2D culture formats. Here, we used a fully defined, 3D, thermoresponsive biomaterial platform to rapidly generate large numbers of action-potential firing mDA neurons after 25 days of differentiation (~40% tyrosine hydroxylase (TH) positive, maturing into 25% cells exhibiting mDA neuron-like spiking behavior). Importantly, mDA neurons generated in 3D exhibited a 30-fold increase in viability upon implantation into rat striatum compared to neurons generated on 2D, consistent with the elevated expression of survival markers FOXA2 and EN1 in 3D. A defined, scalable, and resource-efficient cell culture platform can thus rapidly generate high quality differentiated cells, both neurons and potentially other cell types, with strong potential to accelerate both basic and translational research.